## REMARKS

Claims 113, 117-120, 123, 125, 129-135, 137-139, 141-144, 170-174, 180-182, 185, 187, 190-195, 197-204, 206-209, 235-239, 241-244, 247-251 and 254-257 constitute the pending claims in the present application. Claims 243, 244 and 247-250 have been withdrawn by the Examiner as being directed to non-elected inventions.

Support for the amendments and new claims can be found throughout the instant specification and claims as filed.

Applicant asserts that no new matter has been added to the specification or claims. Applicant reserves the right to prosecute any cancelled subject matter in a future application.

Applicant respectfully requests reconsideration of the rejections of record in view of the following remarks. Issues raised by the Examiner are addressed below in the order they appear in the Office Action.

### *35 U.S.C. § 102(e)*

Claims 113, 117-120, 123, 131-135, 137-139, 141-144, 170-175, 180-182, 185, 190, 193-204, 206-209, and 235-239 remain rejected and new claims 240-242, 245-246, and 251-253 are rejected under 35 USC § 102(e) as allegedly being anticipated by U.S. Patent No. 5,532,159 (Webb et al., filed April 1, 1994; the "'159 Patent") for the reasons of record in the Action mailed September 25, 2003.

The Examiner stated at page 4 of the Office Action that the inventors' (i.e., the '159 inventors) "belief" does not remove the possibility that other mechanisms are responsible for the observed anti-tumor effects of the anti-OFP antibodies. It appears that the Examiner is stating that the '159 inherently teaches the claimed invention even though it sets forth a completely different mechanism that the findings disclosed in the present specification.

Applicants respectfully disagree for the reasons of record and those set forth herein.

The present claims require a method for inducing a therapeutic host immune response against a multi-epitopic *in vivo* antigen that does not elicit an effective host immune response, and eliciting an effective host T cell or humoral immune response.

Applicants respectfully submit that at no point has the Examiner established that the '159 patent even contemplates a method for inducing a therapeutic host humoral immune response or a therapeutic host T cell response for the following reasons.

1. It is well established in the field of immunology that there are two general types of immune responses: (1) a humoral immune response mediated by B lymphocytes and antibodies and (2) a cellular immune response mediated by T lymphocytes. Induction of an immune response includes activation, proliferation and differentiation of B and T cells, and may also include migration of cells within the body.

2. The decrease in tumor volume in the '159 patent begins almost immediately as shown in Figure 1, wherein the anti-OFP antibody is administered on **day 7** of the protocol, and tumor volume is decreased on **day 8** (i.e., a one-day induction period).

3. It is well established that induction of a humoral immune response includes both a primary and secondary antibody response. The primary "antibody response is detected ***5-10 days*** after antigen injection, rises over the next ***10-20 days***, and then declines to a low level without ever completely disappearing. If the same antigen is administered again several weeks later, a secondary antibody response the antibody response is more rapid, hits a higher peak level, and declines, but to a higher baseline level than previously seen." Emphasis added. See Figure 4.9, Peakman and Vergani, Basic and Clinical Immunology, Churchill Livingstone, 1997, pp. 41-42 (Exhibit A). Thus, induction of a humoral immune response would not result in an effect within 1 day after antigen injection.

4. It is well established that induction of a cellular immune response takes more than one day.

    - Thaler et al. (Medical Immunology, Ed. J.B. Lippincott Company, 1977, pp. 23-25 and 28; Exhibit B) teach that injection of antigen leads to blast-cell activity in the T-cell paracortical areas by ***two days***, and ***several days later***,

follicular activity is noted and germinal centers are formed (i.e., beginning stages of a host T cell response; see left column of page 23).

- Durkin and Waksman (*J. Immunol.*, 1975 Jul; 115(1): 170-176) (Exhibit C) teach that lymph node cells such as T lymphocytes in response to the antigen, OA, ***first appeared*** in culture at ***day 5*** and peaked at day ***9 to 12 days***. (See Figures 1 and 2 and description at right column of page 172)

Applicants submit that the antibodies of the '159 Patent and the binding agents of the instant application are fundamentally different. Consequently, the method steps described in the prior art do not comprise the same steps as claimed in the instant application, and the claimed functional limitations are not an inherent property of the referenced method. The claims do recite a material difference as compared to the cited art, and are distinguished over the prior art teaching. As described above, induction of an immune response, whether humoral or cellular or both, takes more than one day to develop, and thus cannot be the cause of the effect recognized in the '159 Patent.

A reference cannot inherently anticipate the claims unless it teaches every aspect of the claimed invention. In the instant case, the decrease in tumor volume observed in the '159 Patent cannot possibly be due to induction of an effective host immune response as is required by the instant claims. Thus, Applicants submit that the anti-OFP antibodies of the '159 Patent do not inherently anticipate the instant claims.

Applicants respectfully request reconsideration and withdrawal of the rejection.

***35 U.S.C. § 103(a)***

Claims 113, 117-120, 123, 125, 129-135, 137-139, 141-144, 170-175, 180-182, 185, 187, 190-204, 206-209 and 235-239 remain rejected and new claims 240-242, 245-246 and 251-257 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Baum et al. (Hybridoma, 12(5): 583-589 (1993)) or Madiyalakan et al. (Hybridoma 14(2): (1995)) in further

view of U.S. Patent 5,532,159 (Webb et al., filed April 1, 1994) for the reasons of record in the Action mailed September 25, 2003.

The Examiner stated at page 5 of the Office Action that the motivation to combine the references was provided by the '159 Patent.

Applicants respectfully disagree for the reasons of record and for those stated above. The deficiencies of the '159 Patent have been discussed *supra,* and this reference cannot cure the deficiencies of Baum et al. or Madiyalakan et al.

Applicants assert that Baum et al., Madiyalakan et al. and the '159 Patent do not teach or suggest all of the limitations of the instant claims, nor do not they provide any motivation to arrive at the invention as currently claimed.

Applicants respectfully request reconsideration and withdrawal of the rejection.

***35 U.S.C. § 112, 1st paragraph***

The specification remains objected to and claims drawn to specific biological deposits (i.e., Claims 125, 187) remain rejected for the reasons of record for not stating that all restrictions upon public access will be removed upon grant of a patent.

Applicant hereby state that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be maintained for the required time and replaced if viable samples cannot be dispensed by the depository if required.

**New objections/rejections**

***Claim objections***

Claims 125 and 187 are objected to for reciting "produceable," which is spelled incorrectly. Claims 125 and 187 have been amended to correct the spelling error.

Claims 240, 245, and 246 are objected to as being substantial duplicates of claims 142, 143, and 144, respectively. Applicants have cancelled claims 240, 245, and 246, thereby obviating the objection.

***35 U.S.C. § 112, first paragraph, written description***

Claims 190 and 238 are rejected, as the specification allegedly does not contain a written description of "non-human" antibody.

Applicants submit that the specification as filed provides sufficient support and guidance to "non-human" antibodies, such as B43.13 (i.e., a murine monoclonal antibody) which are administered to human patients. See, for example, lines 5-6 of page 19, pages 23-28, and Example 1 of the specification. What is well known in the art need not be described in detail. Further, the subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to meet the written description requirement. MPEP § 2163.02.

Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

Date: May 17, 2004

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